

Docket No. 434-400 DIV

Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:
MUMPER ET AL.	: Confirmation No.: 5127
	: Group Art Unit: 1618
	: Examiner: Rogers, James W.
Serial No.: 10/072,320	:
	:
Filed: Feb. 7, 2002	:

For: Ph-SENSITIVE MUCOADHESIVE FILM-FORMING GELS AND WAX-FILM
COMPOSITES SUITABLE FOR TOPICAL AND MUCOSAL DELIVERY OF
MOLECULES

APPEAL BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appeal is taken from the rejections made in the January 14, 2011 Office Action. No claim has been allowed. Claims 33-34, 42-46, 51, 56-57, and 63-68 remain pending, stand at least twice-rejected, and are appealed herein. A timely Notice of Appeal, pre-Appeal Brief Request for Review, and fee were submitted to the Office on March 14, 2011. The Notice of Panel Decision from Pre-Appeal Brief Review mailed on April 15, 2011 set a deadline for filing the Appeal Brief which fell on a Saturday, Sunday, or Federal holiday, and therefore this Brief filed on the next succeeding business day is timely. The Commissioner may charge the Appeal Brief fee [37 C.F.R. §41.20(b)(2)] and any additional fees due and to credit overpayments to the undersigned's **Deposit Account 11-0978**. Remand of the application to the Examiner with instructions for immediate allowance of all pending claims of the application is respectfully requested.

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I. REAL PARTY IN INTEREST

The inventors assigned 100% of their interest in the present application to the University of Kentucky Research Foundation, a corporation of the Commonwealth of Kentucky, having a principal place of business at 311 Main Bldg., University of Kentucky, Lexington, KY 40506-0032. Accordingly, the real party in interest is the University of Kentucky Research Foundation.

II. RELATED APPEALS AND INTERFERENCES

This divisional patent application was the subject of a prior appeal. Namely, after a final Office Action mailed on November 17, 2004 rejecting all pending claims, an Appeal Brief was filed by the present Appellant on June 20, 2005 and subsequently a Reply Brief to the Examiner's Answer was filed on December 20, 2005. On Appeal, the Board found in favor of the Appellant and reversed the Examiner on all counts (see *Ex parte* Russell Mumper and Michael Jay, Appeal No. 2008-2332, decided June 27, 2008).

The Appellant knows of no other prior or pending appeals, interferences, or judicial proceedings, which may be related to, directly affect, or be directly affected by, or have a bearing on, the Board's decision in this Appeal.

III. STATUS OF THE CLAIMS

Claims 33-34, 42-46, 51, 56-57, and 63-68 remain pending, stand at least twice-rejected, and are appealed herein. Claims 33 and 66-68 are independent. Claims 47-50 and 52-55 were withdrawn from consideration following a restriction requirement made on November 17, 2004 (see also the Office Action mailed on December 23, 2008). Claims 1-32, 35-41, and 58-62 stand as canceled.

As of the Office Action mailed on January 14, 2011:

1. Claims 33-34, 42-46, 56-57, 65, and 67 stand rejected under 35 U.S.C. §103(a) over U.S. Patent No. 6,270,783 to Slavtcheff et al. ("Slavtcheff") in view of U.S. Patent No. 4,715,369 to Suzuki et al. ("Suzuki");
2. Claims 33-34, 42-46, 51, 56-57, and 63-68 stand rejected under 35 U.S.C. §103(a) over Slavtcheff in view of Suzuki, further in view of U.S. Patent No. 6,562,363 to Mantelle et al. ("Mantelle"); and
3. Claims 33-34, 42-46, 56-57, and 63-67 stand rejected under 35 U.S.C. §103(a) over Mantelle in view of Suzuki.

On appeal, the Appellant respectfully requests reversal of the rejections of all pending claims.

IV. STATUS OF AMENDMENTS

No amendment has been filed subsequent to the Office Action dated January 14, 2011 and the Notice of Appeal filed on March 14, 2011, and all previous amendments have been entered. The form of the claims for purposes of Appeal are those presented in the Amendment and Response electronically filed by the Appellant on November 3, 2010. As required, a copy of the claims is included herewith in the Claims Appendix, *infra*.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Parenthetical cites to the specification of the present application are provided to supply and/or supplement the required concise summary of the claimed subject matter, are representative in nature, and do not represent the only portion of the disclosure wherein support for the claim limitation is provided. Claims 33-34, 42-46, 51, 56-57, and 63-68 remain pending and are appealed herein. Claims 33 and 66-68 are independent. Claims 47-50 and 52-55 were withdrawn from consideration following a restriction requirement made on November 17, 2004, and claims 1-32, 35-41, and 58-62 were previously canceled. Therefore, those claims are not set forth or discussed in this section, but are provided for the Board's convenience in the Claims Appendix.

In the claims, and consistent with the Figures, for example, the below-limitations are representatively found in the specification at least at the concise parenthetical cite.

33. A bi-layer wax-film composite (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*) having a total thickness of less than 5 mm (*pg 8, 2d full ¶; pg 12 1st full ¶*), comprising:

(a) a pH-sensitive mucoadhesive layer (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*), comprising:

(1) at least one water-insoluble swellable anionic (*Appellant's specification, pg 25, 1st full ¶: "Noveon and Carbomer-based polymers are weak acids and contain many negatively charged carboxyl groups"*) mucoadhesive polymer (*Appellant's specification, pg 5 2d full ¶*); and

(2) at least one anionic (*Appellant's specification, pg 17 at top*) pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester (*Appellant's specification, pg 5 2d and 3d full ¶¶; pg 6*

3d full ¶; pg 16-17, ¶ beginning with Eudragits® are synthetic ..., see esp. pg 17 at top);

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer (*Appellant's specification pg 7, 1st full ¶; pg 7 final partial paragraph bridging to pg 8; pg 18, second full ¶*); and

(c) at least one molecule of interest (*Appellant's specification, pg 5 2d full ¶; pg 6 1st full ¶*);

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto (*Appellant's specification pg 5, 1st full ¶*).

34. The wax-film composite of claim 33, wherein the pH-sensitive mucoadhesive layer is present at a concentration of 20% to 90% by weight, and the water-insoluble wax layer is present at a concentration of 10% to 80% by weight (*Appellant's specification pg 7, 1st full ¶*).

42. The wax-film composite of claim 33, wherein the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax having a melting point between 40° C and 100° C and at least one water-soluble or water-swellaable polymer (*Appellant's specification pg 7, 4th full partial ¶*).

43. The water-insoluble pharmaceutical wax of claim 42, wherein said wax is beeswax, emulsifying wax, microcrystalline wax, carnauba wax, paraffin wax, white wax, yellow wax, or other suitable pharmaceutical wax (*Appellant's specification pg 7, final partial ¶; pg 18, 1st full ¶*).

44. The water-soluble or swellable polymer of claim 42, wherein said polymer is present in the insoluble wax layer at a concentration from 0.05% to 10% by weight (*Appellant's specification pg 7, final partial ¶*).

45. The water-soluble or swellable polymer of claim 42, wherein said water-soluble or water-swallowable polymer is tragacanth, polyvinyl pyrrolidone, polyvinyl alcohol, cross-linked polyacrylic acid, polyethylene glycol, a cellulose polymer derivative, or other suitable pharmaceutical polymer that is water-soluble or water-swallowable (*Appellant's specification pg 7, final partial ¶ bridging to pg 8*).

46. The wax-film composite of claim 33, wherein the molecule of interest is contained in and released from either the pH-sensitive mucoadhesive layer or the water-insoluble wax layer (*Appellant's specification pg 8, top partial ¶*).

51. The wax-film composite of claim 33, wherein the molecule of interest is a peptide or protein (*Appellant's specification pg 8 1st full ¶; pg 12, final partial ¶*).

56. The wax-film composite of claim 33, wherein the wax-film composite is applied to an application site comprising: the skin, mouth, vagina, nasal cavity, or other accessible mucosal site (*Appellant's specification pg 8, 2d full partial ¶*).

57. The wax-film composite of claim 56, wherein the wax-film composite adheres to the application site for at least one hour (*Appellant's specification pg 8, 2d full partial ¶; pg 19, 1st partial ¶*).

63. The wax-film composite of claim 33, wherein the weight ratio of water-insoluble swellable anionic mucoadhesive polymer to anionic pH-sensitive film-forming

copolymer is from 2:1 to 4:1 (*Appellant's specification Fig. 3, Examples 2, 3, 5, 7, 8, and others*).

64. The wax-film composite of claim 47, wherein the active pharmaceutical compound is an antimicrobial, an antiviral, an antiinflammatory, an antiseptic, an antihistamine, a local anesthetic, a disinfectant, a keratolytic, an analgesic, an anti-migraine or an antifungal (*Appellant's specification pg 12, final partial ¶*).

65. The wax-film composite of claim 33, wherein the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax having a melting point between 40° C and 100° C (*Appellant's specification pg 7, 4th full ¶*).

66. A bi-layer wax-film composite (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*) having a total thickness of less than 5 mm (*pg 8, 2d full ¶; pg 12 1st full ¶*), comprising:

(a) a pH-sensitive mucoadhesive layer (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*), comprising:

(1) at least one water-insoluble swellable anionic (*Appellant's specification, pg 25, 1st full ¶: "Noveon and Carbomer-based polymers are weak acids and contain many negatively charged carboxyl groups"*) mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol (*Appellant's specification, pg 5 2d full ¶; pg 7, 2d full ¶*); and

(2) at least one anionic (*Appellant's specification, pg 17 at top*) pH-sensitive film-forming polymer copolymer of methacrylic acid and acrylic or methacrylic ester (*Appellant's specification, pg 5 2d and 3d full ¶¶; pg*

6 3d full ¶; pg 16-17, ¶ beginning with Eudragits® are synthetic ..., see esp. pg 17 at top);

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer (*Appellant's specification pg 7, 1st full ¶; pg 7 final partial paragraph bridging to pg 8; pg 18, second full ¶*); and

(c) at least one molecule of interest (*Appellant's specification, pg 5 2d full ¶; pg 6 1st full ¶*);

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto (*Appellant's specification pg 5, 1st full ¶*).

67. A bi-layer wax-film composite (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*) having a total thickness of less than 5 mm (*pg 8, 2d full ¶; pg 12 1st full ¶*), comprising:

(a) a pH-sensitive mucoadhesive layer (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*), consisting essentially of:

(1) at least one water-insoluble swellable anionic (*Appellant's specification, pg 25, 1st full ¶: "Noveon and Carbomer-based polymers are weak acids and contain many negatively charged carboxyl groups"*) mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol (*Appellant's specification, pg 5 2d full ¶; pg 7, 2d full ¶*); and

(2) at least one anionic (*Appellant's specification, pg 17 at top*) pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester (*Appellant's specification, pg 5 2d and 3d full ¶¶; pg 6 3d full ¶; pg 16-17, ¶ beginning with Eudragits® are synthetic ..., see esp. pg 17 at top*);

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer (*Appellant's specification pg 7, 1st full ¶; pg 7 final partial paragraph bridging to pg 8; pg 18, second full ¶*); and

(c) at least one molecule of interest (*Appellant's specification, pg 5 2d full ¶; pg 6 1st full ¶*);

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto (*Appellant's specification pg 5, 1st full ¶*).

68. A bi-layer wax-film composite (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*) having a total thickness of less than 5 mm (*pg 8, 2d full ¶; pg 12 1st full ¶*), comprising:

(a) a pH-sensitive mucoadhesive layer (*Appellant's specification pg 8 bridging to pg 9, ¶ beginning with "A wax-film composite..."*), consisting of:

(1) at least one water-insoluble swellable anionic (*Appellant's specification, pg 25, 1st full ¶: "Noveon and Carbomer-based polymers are weak acids and contain many negatively charged carboxyl groups"*) mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol (*Appellant's specification, pg 5 2d full ¶; pg 7, 2d full ¶*); and

(2) at least one anionic (*Appellant's specification, pg 17 at top*) pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester (*Appellant's specification, pg 5 2d and 3d full ¶¶; pg 6 3d full ¶; pg 16-17, ¶ beginning with Eudragits® are synthetic ..., see esp. pg 17 at top*);

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer (*Appellant's specification pg 7, 1st full ¶; pg 7 final partial paragraph bridging to pg 8; pg 18, second full ¶*); and

(c) at least one molecule of interest (*Appellant's specification, pg 5 2d full ¶; pg 6 1st full ¶*);

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto (*Appellant's specification pg 5, 1st full ¶*).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Board is respectfully requested to determine whether claims 33-34, 42-46, 56-57, 65, and 67 are rendered obvious by U.S. Patent No. 6,270,783 to Slavtcheff et al. ("Slavtcheff") in view of U.S. Patent No. 4,715,369 to Suzuki et al. ("Suzuki"). Likewise, the Board is respectfully requested to determine whether claims 33-34, 42-46, 51, 56-57, and 63-68 are obvious over the teachings of Slavtcheff in view of Suzuki, further in view of U.S. Patent No. 6,562,363 to Mantelle et al. ("Mantelle"). Finally, the Board is respectfully requested to determine whether claims 33-34, 42-46, 56-57, and 63-67 are rendered obvious by Mantelle in view of Suzuki.

In making these determinations, the Board is respectfully requested to determine: a) whether the cited references teach or in any way suggest each and every claim limitation as advocated by the Examiner; b) whether the Examiner has met his *prima facie* burden of articulating a reason that the skilled artisan would consider combining the teachings of the references to provide each and every limitation of the present claims in the manner claimed by the Appellant; and c) whether the skilled artisan, on examining the cited prior art, would be provided a reasonable expectation of success of the combinations advocated by the Examiner.

To the extent the Board's determination finds any of the above in favor of the Appellant, the entirety of the claims should be adjudicated patentable in view of the pending rejections.

VII. ARGUMENT

A. PRELIMINARY REMARKS.

As summarized in Section II of this paper, this application has appeared before the Board previously, for adjudication of remarkably similar issues. Referring to the Board's decision in *Ex parte* Russell Mumper and Michael Jay,¹ the Office in that case relied on recitations use of Eudragit polymethacrylate copolymers and of Carbopol 934 in U.S. Patent No. 5,700,478 to Biegajski combined with a teaching of a drug delivery device made of a wax layer comprising layers made of polymers (e.g. Carbopol) in U.S. Patent No. 4,959,218 to Eckenhoff. Despite the fact that neither reference taught or in any way suggested making wax-film composites comprising a pH-sensitive mucoadhesive layer and a water-insoluble wax layer as then claimed by the Appellants, the Office reached a conclusion of obviousness. The Board properly found this conclusion to be unsupported and reversed the obviousness rejection (*pg* 7 of the opinion).

In the current Appeal, the Office once again relies on references which teach generally known compositions sold under various trademarks including Eudragit, Carbopol, Carbomer, and others, but which neither teach nor in any way suggest pH-sensitive mucoadhesive layers bonded to pharmaceutical wax layers as claimed by the Appellants, and yet again finds legal obviousness. The Board is respectfully requested to again find that the Office's position lacks support, and that no reference relied on by the Examiner teaches or in any way suggests a bi-layer wax-film composite comprised of a pH-sensitive mucoadhesive layer (at least one pH-sensitive film forming polymer and at least one water-insoluble mucoadhesive polymer) bonded to a water-insoluble wax layer as claimed by the Appellants.

¹ Appeal 2008-2332, decided June 27, 2008.

B. THE REJECTION OF CLAIMS 33-34, 42-46, 56-57, 65, AND 67 UNDER 35 U.S.C. §103(A) OVER SLAVTCHEFF AND SUZUKI.

1. Applicable law.

Findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E).² Moreover, the Federal Circuit Court of Appeals has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by “substantial evidence” within the record.³ Thus, in order to uphold the Examiner’s position on Appeal, the Board must find that that the position is supported by substantial evidence in order to affirm.

In turn, to find *prima facie* obviousness, even post-*KSR* it remains a requirement that the references teach or suggest each and every claim limitation, that the skilled artisan be provided some objective reason for arriving at each and every claim limitation, and that the skilled artisan be afforded a reasonable expectation of success of combining the prior art teachings to provide each and every claim limitation. Merely pointing to the presence of claim elements in the prior art does not suffice as a complete statement of a rejection for obviousness.⁴ Rather, a rejection of claims based on the rationale that the claimed invention is a combination of prior art elements also requires a finding that the results flowing from the combination would have been suggested and predictable to the skilled artisan.⁵

² *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999).

³ *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000) (“... the ‘substantial evidence’ standard asks whether a reasonable fact finder could have arrived at the agency’s decision.” *Id.* at 1312).

⁴ Examination Guidelines Update: Developments in the Obviousness Inquiry after *KSR v. Teleflex*, Fed. Reg. Vol. 75, No. 169, Sept. 1, 2010, citing *Crocs, Inc. v International Trade Commission*, 598 F.3d 1294 (Fed. Cir. 2010).

⁵ *Id.*, see also Manual of Patent Examining Procedure §2143 A(3). To reject a claim as *prima facie* obvious based on features disclosed in one or more references, there must be some suggestion, either in the art itself or in the knowledge available to the skilled artisan, of the desirability of making the combination (Manual of Patent Examining Procedure ch. 2100, Section 2143.01, p. 131: “The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the

Admittedly, under the current guidelines an “obvious to try” rationale, that is, combining selected elements from one or more prior art references without an express rationale provided by the references, can support a rejection under 35 U.S.C. §103 under certain circumstances.⁶ However, even under *KSR* and post-*KSR* case law, this only applies when there are a “finite number of identified, predictable solutions, *with a reasonable expectation of success*” (emphasis added), and the *KSR* requirement for providing an objective reason leading the skilled artisan to combine references remains. That is, the requirement of a reasonable expectation of success remains, even when the particular facts permit an “obvious to try” analysis for legal obviousness.⁷

In the present case, however, the skilled artisan is not faced with a “finite number of identified, predictable solutions, coupled with a reasonable expectation of success leading inexorably to a supportable holding of *prima facie* obviousness of a pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming copolymer and a pharmaceutical wax

combination.”) (Emphasis in original). Still further, it is required that a reasonable expectation of success support the finding of obviousness. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986). Thus, the *prima facie* case of obviousness is established only when the teachings from the prior art, the knowledge available to the skilled artisan, or a combination thereof would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Bell*, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). Also, despite any recent revisions to the MPEP, it remains a requirement to a finding of obviousness that the prior art reference or references must teach or suggest all the claim limitations. Manual of Patent Examining Procedure §2143. This test for *prima facie* obviousness is consistent with the legal principles set forth in *KSR Int’l Co. v. Teleflex Inc.* (127 S.Ct. 1727 (2007), 82 USPQ2d 1385 (2007). Summarizing the Supreme Court’s holding in that case, the Federal Circuit Court of Appeals noted that “... the Court acknowledged the importance of identifying ‘a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does’ in an obviousness determination.” *Takeda Chemical Industries Ltd. v. Alphapharm Pty.*, 83 USPQ2d 1169 (Fed. Cir. 2007) (quoting *KSR*, 127 S. Ct. at 1731). When determining whether a claim is obvious, an Examiner must make “a searching comparison of the claimed invention - *including all its limitations* - with the teaching of the prior art.” *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Moreover, “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

⁶ See, Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. 72, No. 195, 57526-57535, at pg. 57529.

⁷ *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc. and Mylan Pharmaceuticals, Inc.*, (2007-1223 (Fed. Cir. 2008) (“... the passage in *KSR* posits a situation with a finite, and in the context of the art,

bonded to the pH-sensitive mucoadhesive layer, for delivering a molecule of interest to mucosa as claimed. Rather, the skilled artisan is provided only a lengthy list of ingredients spanning multiple columns of text (for example, see Slavtcheff *Col. 4-7*), with no reason articulated for the skilled artisan to consider any particular combination thereof to arrive at the Appellant's precisely claimed pH sensitive mucoadhesive layer bonded to a pharmaceutical wax layer, for delivering a molecule of interest to mucosa, other than the guidance provided by the present specification. No element of Slavtcheff and/or Suzuki teaches or articulates an objective reason for the skilled artisan to consider a pH-sensitive mucoadhesive layer bonded to a pharmaceutical wax layer and including at least one water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film forming polymer as expressly claimed herein, that forms films when applied to a surface due to changes in pH and desolvation of polymer, further wherein that pH-dependent film-forming property provides for delivery of a molecule of interest to or through the application site (Appellant's specification, at least at *pg 6*, second full ¶). The rejections should be reversed.

2. The references do not teach or suggest each limitation of independent claims 33 and 67 or provide a reasonable expectation of success.

The independent claims under appeal are directed to a bi-layer wax-film composite of a defined thickness, for delivering a molecule of interest to a mucosal surface. The wax-film composite comprises a pH-sensitive mucoadhesive layer and a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer. The pH-sensitive mucoadhesive layer in turn comprises at least one water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film forming polymer. As is clear from the Appellant's specification, the pH-sensitive mucoadhesive layer forms films when applied to a surface due to changes in pH and

small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness."); *see also Takeda Chemical Industries Ltd. v. Alphapharm Pty.*, 83 USPQ2d 1169 (Fed. Cir. 2007).

desolvation of polymer, whereby that pH-dependent film-forming property provides for delivery of a molecule of interest to or through the application site (Appellant's specification, at least at *pg* 6, second full ¶) from either of the pH-sensitive mucoadhesive layer or the pharmaceutical wax layer (Appellant's specification, *pg* 8, first partial paragraph, see also claim 46).

The Examiner maintains that the above claims are obvious over the teachings of Slavtcheff in view of Suzuki. Turning to the teachings of the primary reference, nowhere does Slavtcheff teach or hint at combining compositions to provide a pH-sensitive anionic mucoadhesive polymer for delivery of a molecule of interest as is expressly claimed by the Appellants. Instead, Slavtcheff teaches only a temperature-sensitive dermo-adhesive layer comprising liquid crystal thermochromic substances (*Col. 2, ll* 25-65) wherein a water-interactive agent induces a temperature change of at least 2 ° C (*Col. 2, ll* 15-17) which causes the thermochromic substances to change color to provide a visual indicator to the consumer that the dermal strip has been in place for a sufficient period of time. There is simply no indication in Slavtcheff of any need or reason for pH-sensitivity, and further no indication that any contemplated composition is capable of delivering a molecule of interest to mucosa. This is to be expected, since the Slavtcheff strip is only intended for removing keratotic plugs from skin pores, rather than for adhering and delivering molecules to mucosal areas.

That is, Slavtcheff exclusively contemplates adhesives for securing a color-changing cosmetic strip (see *Col. 1, ll* 61-63) to skin surfaces (*Col. 3, ll* 1-4), wherein the strip includes compositions providing a visual cue to the user that the strip may be safely removed. This not merely incidental to Slavtcheff's compositions, but rather is required for a primary function of the dermal strip of Slavtcheff, that is, for the adhesive to dry over the area of treatment whereby keratotic plugs adhere to it (*Col. 5, ll* 18-24). The thermochromic compositions provide a color change or "visual sensorial signal" (*Col. 2, ll* 25-26) indicating that the Slavtcheff adhesive strip has been in place for a sufficient

period of time and that the strip may be removed (*Col 1, ll 33-45*: “A sensorial signal would be helpful for the consumer to know when to begin the peel removal”).

Suzuki is cited for a teaching of thin layers for adhesive patches and for use of a wax backing layer. No other teaching of Suzuki appears relevant to the present claims. Indeed, Suzuki’s teaching of a composition “*consisting essentially of* a cellulose lower alkyl ether and a polyacrylic acid or pharmaceutically acceptable salt thereof (emphasis added; see Suzuki *Abstract*), in fact appears to exclude the presently claimed pH-sensitive mucoadhesive polymer.⁸ Further, in the Office Action mailed on December 23, 2008 (*pg 6*), the Examiner conceded that Suzuki did not teach specific film formers as recited in the Appellants independent claims.

The Examiner cites Suzuki (*pg 4* of the Office Action mailed on December 23, 2008) for teaching a non-adhesive layer made from a variety of constituents including bees wax (see Suzuki *Abstract, Col. 2, ll 14-22, and Col. 5, line 44-Col. 6, line 3*). Suzuki teaches a “... two layer tablet having a nonadhesive layer” to prevent involuntary adhesion of the preparation to “... an undesired part” (*Col. 5, ll 44-47*). Bees wax is mentioned only at *Col. 6, line 3*. Regardless, the Board’s attention is directed to the specific claim limitation in question (see claim 33 representatively), reciting a water-insoluble pharmaceutical wax layer *bonded to the pH-sensitive mucoadhesive layer* (emphasis added). See also the Appellant’s specification at least at *pg 18*, second full paragraph: “A wax-film composite refers to a bi-layer film comprised of a pH-sensitive mucoadhesive layer and a water-insoluble wax layer ... For bonding the two layers of the bi-layer wax-film composite, it is preferred that the water-insoluble wax layer contain at least one water-soluble or water-swellaable agents ...”

⁸ See, Manual of Patent Examining Procedure §2111.03, noting that the transitional phrase “consisting essentially of” is interpreted to be limiting to those materials or steps that do not materially affect the basic and novel characteristics of the claimed invention.

Thus, the present claims require that the water-insoluble wax layer be bonded to the pH-sensitive mucoadhesive layer. Of course, while limitations cannot be imported into the claims from the specification, it is required that a claim be interpreted according to its definition in the specification,⁹ and it will be appreciated that this particular claim limitation read in light of the Appellant's specification defines a bonding allowing the subsequently claimed molecule of interest to be contained in and delivered from either the anionic pH-sensitive film-forming copolymer or the pharmaceutical wax layer (Appellant's specification, pg 8, first partial paragraph, also claim 46).

Contra, Suzuki teaches only an adhesive layer plus a nonadhesive layer (which may be bees wax or other compositions) to prevent inadvertent adherence, with no indication that any contemplated nonadhesive composition is or could be formulated to deliver a composition. While Suzuki does teach application of pressure whereby "... the two layers are tightly bound together and will not hardly separate from each other, thus increasing the yield" (*Col. 6, ll 25-30*), there is no element of bonding taught or in any way suggested by Suzuki whereby an active ingredient may be delivered from either of the bioadhesive layer or the wax layer, or any suggestion that such would be at all desirable for Suzuki's tablets. Rather, Suzuki merely contemplates a nonadherent covering layer (Suzuki *Col. 5, ll 32-36*: "... a two-layer tablet comprising a covering material ... a nonadhesive layer which has no adhesion to the wet oral mucosa.") to prevent inadvertent and undesirable adherence of its tablets, and further appears to expressly exclude delivery of a medicament or other molecule of interest from its nonadherent layer (Suzuki claim 1: "... a medicament-free nonadherent layer...").

⁹ *Liquid Dynamics Corp. v. Vaughan Co.*, 355 F.3d 1361, 1367 (Fed. Cir. 2004), citing *Vitronics Corp. v. Conceptor, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("The specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication"); *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005); *In re Suitco Surface, Inc.*, 2009-1418, Reexamination no. 90/007,015 (Fed. Cir. 2010) ("... this court has instructed that any such [claim] construction be 'consistent with the specification' ... and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art," citing *In re*

Slavtcheff lacks any teaching or suggestion at all of a pharmaceutical wax layer bonded to a pH-sensitive mucoadhesive layer. Thus, this limitation of the Appellant's claims is neither taught nor suggested by the references.

Other than Suzuki's nonadhesive layer or coating, the rejection appears to rely solely on the Slavtcheff recitation of various compositions known in the art, including monomers such as methacrylic acid (*Col. 4, ll 51-54*), but also trademarks such as Carbomer® (*Col. 5, ll 15-17*) and others (see *Col. 5* and *Col. 6*), for use in dermal adhesives, rather than any reason articulated by Slavtcheff/Suzuki or the knowledge in the art leading the skilled artisan to consider combining any of the ingredients to provide the particular pH-sensitive mucoadhesive polymers of the present disclosure.

With regard to the Examiner's reliance on recitation of trademarks, in dismissing the Appellant's prior arguments, the Examiner previously stated (in reference to the trademark Carbomer®) that "[T]he same compound is the same no matter what the name is given to the compound" (Office Action mailed January 14, 2011, *pg 4*, see also the Office Action mailed on August 16, 2010, *pg 5*, at bottom) (as will be discussed below, the Examiner makes similar broad statements in relation to the trademarks Eudragit® and Noveon®). The "same compound" may be the "same compound," but that is not the basis for the Examiner's rejection. Rather, from the above statement the rejection appears to be based at least partially on the Examiner's belief that the same trademark or same trade name must be the same compound. For an accurate record, this simply cannot be the case, at least because it is well known that various compositions having markedly dissimilar properties are often marketed under the same brand name. Further, as stated by the Examiner himself in rejecting claims as indefinite (*pg 3* of the Office Action mailed on August 16, 2010), a "... trademark or trade name cannot be used properly to identify any particular material or product." Even more, with reference to the term

carbomer when not used as a mark, the skilled artisan is aware that the name does not refer to a single polymer, but rather is generically applied to a line of synthetic high molecular weight polymers of acrylic acid which are assigned various codes (910, 934, 940, and 934P, for example) to reflect differences in molecular weight and specific components of the polymer line. As such, the Slavtcheff use of the trademarks without more does not provide sufficient guidance to the skilled artisan to support *prima facie* obviousness.

Also, as is well known to the skilled artisan in the chemical arts, mixing of even the same ingredients, in different proportions and/or under different conditions, can lead to compositions having very different and unexpected properties. For that reason, even if one were to accept that Slavtcheff/Suzuki teach or suggest every limitation of the Appellant's independent claims (which they do not), the references fail to supply the requisite expectation of success that is a necessary underpinning of any finding of obviousness.

3. The references articulate no objective reason for the skilled artisan to combine particular compositions taught by Slavtcheff or Suzuki to arrive at the limitations of the independent claims.

In addition to failing to teach or suggest a pH-sensitive mucoadhesive layer bonded to a pharmaceutical wax layer as claimed by the Appellants, the mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film forming polymer, it cannot fairly be said that any teaching of Slavtcheff/Suzuki articulates any reason for the skilled artisan to consider combining the recited compositions to provide a pH-sensitive anionic mucoadhesive polymer bonded to a pharmaceutical wax layer, to deliver a molecule to mucosa as claimed. At most Slavtcheff/Suzuki motivate the skilled artisan to consider combinations providing adhesives for adhering to skin and which change color to cue the user that a blemish may be removed.

The Examiner points to no element of Slavtcheff/Suzuki teaching or articulating any objective reason for considering combining any of the three-column long list of compositions (Slavtcheff *Col. 4-7*) to provide a pH-sensitive anionic mucoadhesive polymer for delivering a molecule to mucosa, but rather merely picks out individual elements of the Appellant's claims from the references and finds their combination in the manner taught by the Appellants obvious. No teaching of the references leads the skilled artisan to consider any issue of or requirement for the presently claimed properties of pH sensitivity and mucoadherence. Even further, there is no indication in Slavtcheff/Suzuki leading the skilled artisan to consider the particular combination of a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming polymer, to provide such a pH-sensitive anionic mucoadhesive polymer bonded to a pharmaceutical wax layer as claimed for delivering a molecule to mucosa.

Moreover, as noted above Suzuki is adamant in its teaching of a completely nonadherent layer which may be a bees wax. Slavtcheff teaches only an adhesive comprising a thermochromic composition, for providing a visual cue to the user. In order for the combination advocated by the Examiner to function, that is, the combination of Slavtcheff's thermochromic adhesive and Suzuki's nonadherent layer wherein the nonadherent layer prevents inadvertent adherence as taught by Suzuki but the adherent layer binds to skin for removal of keratin plugs as taught by Slavtcheff, clearly the Suzuki nonadherent layer would have to be superposed on top of Slavtcheff's thermochromic adhesive layer. Doing so would prevent a primary function of Slavtcheff's thermochromic layer, i.e., providing the visual cue, unless the nonadherent layer was transparent (which Suzuki does not teach or in any way suggest). Of course, advocating modifications to a composition to support an obviousness position which render that composition incapable of performing its intended function remains improper.¹⁰ As such,

¹⁰ *In re Ratti*, 270 F.3d 810, 123 USPQ 349 (CCPA 1959).

the skilled artisan would not be motivated to combine compositions as taught by Slavtcheff and Suzuki, since doing so would obscure the visual cue which the Slavtcheff adhesive was designed to provide.

As the law has long provided, “[t]he Patent Office has the initial duty of supplying the factual basis for its rejection. *It may not, because it may doubt that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis.* To the extent the Patent Office rulings are so supported, there is no basis for resolving doubts against their correctness. *Likewise, we may not resolve doubts in favor of the Patent Office determination when there are deficiencies in the record as to the necessary factual bases supporting its legal conclusion of obviousness*”¹¹ (emphasis added). To simply select elements from otherwise unrelated portions in the references to arrive at the claimed composition, without some objective reason for doing so supplied by the references or the knowledge in the art, amounts to impermissible hindsight reconstruction.¹² Selecting particular claim limitations from the prior art to make an obviousness position as the Examiner appears to have done, without providing any rational reason for their combination, has long been discouraged under the law as a form of “hindsight” reconstruction to support a finding of obviousness of claims. In *Graham v. John Deere Co.*,¹³ the U.S. Supreme Court noted that once an invention is known, it makes such combinations seem obvious. The Court cautioned, however, against the practice of “slipping into the use of hindsight”

¹¹ *In re Warner*, 54 C.C.P.A. 1628, 1635 (C.C.P.A. 1967).

¹² *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448 (Fed. Cir. 1986) (“It is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.”); *W.L. Gore Assoc., Inc. v. Garlock, Inc.*, 721 F.3d 1540, 1553 (Fed. Cir. 1983) (“To imbue one of ordinary skill in the art with knowledge of the invention in suit, where no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.”).

¹³ *Graham v. John Deere Co.*, 383 US 1, 36, 148 USPQ 459, 474 (1966).

and urged parties to “resist the temptation to read into the prior art the teachings of the invention in issue.”¹⁴

The references do not teach or suggest each and every limitation of the Appellant’s claims, that is, the presently claimed combination of at least one water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive mucoadhesive polymer to provide a pH-sensitive mucoadhesive layer, further wherein the pH-sensitive mucoadhesive layer is bonded to a pharmaceutical wax layer, all for delivering a molecule of interest. Rather, at most the references suggest a thermochromic adhesive to which one would not want to bond Suzuki’s nonadherent layer, to avoid impairing the intended visual cue. Absent undue experimentation or use of the present Applicant’s specification as a blueprint, each of which is of course improper, no guidance is given to the skilled artisan to arrive at or even consider using any of the Slavtcheff/Suzuki teachings to formulate the Appellant’s claimed subject matter. There is simply no hint or reasoning provided by the references leading the skilled artisan to even consider any issue of pH sensitivity and/or mucoadherence in the resulting compositions, and the Examiner cannot ignore the present claim limitations of pH-sensitivity and mucoadhesiveness, or of a bonded pharmaceutical wax layer, for convenience in making a rejection.

4. Summary

The mere recitation of related compositions, without more, does not provide sufficient teaching or guidance leading the skilled artisan to consider those limitations. Therefore, neither of Slavtcheff, Suzuki, nor any reasonable interpretation of the combined teachings of the references thereof teach or suggest each and every limitation of the present independent claims, nor is any reason articulated that would lead the skilled artisan to use the teachings of the references independently or in combination to

¹⁴ *Id.*

arrive at the presently claimed subject matter. Lacking such teaching or suggestion, it likewise is the case that the skilled artisan is provided no reasonable expectation of success of the presently claimed combination for the purpose of delivering a molecule of interest to mucosa. The *prima facie* case of obviousness is not properly supported as to the independent claims, and the rejection should be reversed.

5. The dependent claims.

Because claim 33 is in condition for allowance, the claims depending from claim 33 are in condition for allowance without consideration of obviousness.¹⁵

Further, claims 34, 42-46, 57, and 65 are believed to be independently patentable because the Examiner has not identified any teaching or suggestion of the cited references believed to render the claims unpatentable. In maintaining the rejection of claims, Examiner refers to prior Office Actions, in particular the Action mailed on October 9, 2009, but consistently appears to focus on application of the teachings of the references primarily to the independent claims. *Prima facie* obviousness is not established with regard to many of the dependent claims, and for this additional reason the rejection should be reversed.

Claim 34, in addition to requiring each limitation of claim 33, recites that “the pH-sensitive mucoadhesive layer is present at a concentration of 20% to 90% by weight, and the water-insoluble wax layer is present at a concentration of 10% to 80% by weight. Lacking substantial evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

Claim 42, in addition to requiring each limitation of claim 33, recites that the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax

¹⁵ *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) (“[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious”); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

having a melting point between 40° C and 100° C and at least one water-soluble or water-swellaable polymer. Lacking any evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

Claim 44, in addition to requiring each limitation of claim 33, recites that the polymer of claim 42 is present in the insoluble wax layer at a concentration from 0.05% to 10% by weight. Lacking any evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

Claim 46, in addition to requiring each limitation of claim 33, recites that the molecule of interest is contained in and released from either the pH-sensitive mucoadhesive layer or the water-insoluble wax layer. As discussed in detail above, Slavtcheff lacks any teaching of a pharmaceutical wax layer at all, and Suzuki expressly teaches against using a wax layer to deliver a molecule of interest. Lacking any evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

Claim 63, in addition to requiring each limitation of claim 33, recites that the weight ratio of water-insoluble swellaable anionic mucoadhesive polymer to anionic pH-sensitive film-forming copolymer is from 2:1 to 4:1. Lacking any evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

Claim 65, in addition to requiring each limitation of claim 33, recites that the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax having a melting point between 40° C and 100° C. Lacking any evidence provided by the Office to show or suggest that this claim is not patentable, *prima facie* obviousness is not supported and the rejection should be reversed.

For these additional reasons, the rejection of claims over Slavtcheff and Suzuki should be reversed.

C. THE REJECTION OF CLAIMS 33-34, 42-46, 51, 56, 57, AND 63-68 UNDER 35 U.S.C. §103(A) OVER SLAVTCHEFF/SUZUKI, FURTHER IN VIEW OF MANTELLE.

The discussion above of applicable law and the teachings of Slavtcheff and Suzuki is incorporated herein by reference as if fully restated. The Examiner takes the position that the above claims are obvious over the teachings of Slavtcheff in view of Suzuki, further in view of Mantelle. Slavtcheff and Sukuki are cited for the propositions addressed above. Mantelle is cited for a teaching of “use of Noveon® and Eudragit® polymers in adhesive compositions for personal use.” (Office Action mailed on 10-9-2009, *pg 6*, restated in subsequent Actions).

1. The references do not teach or suggest each limitation of independent claims 33, 66, 67, and 68 or provide a reasonable expectation of success.

The arguments set forth above discussing the failure of Slavtcheff/Suzuki to support *prima facie* obviousness of the claims likewise apply to the rejection over the combination of Slavtcheff, Suzuki, and Mantelle, the citation to Mantelle for the existence of the known trade names/trademarks Noveon® and Eudragit® and to Slavtcheff for a teaching of Carbomer® (or carbomers) notwithstanding. For the reasons set forth above, Slavtcheff/Suzuki fail to teach or articulate a reason for the skilled artisan to contemplate combinations of compositions providing a pH-sensitive mucoadhesive layer bonded to a pharmaceutical wax layer as expressly claimed by the Appellants for delivery of a molecule of interest to a mucosal surface, the pH-sensitive mucoadhesive layer comprising at least one water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film forming polymer. In turn, those references fail to provide the requisite expectation of success. Inclusion of Mantelle’s recitation of the Noveon® and Eudragit® family of polymers does not salvage the analysis.

The lengthy teaching of ingredients set forth at least in Slavtcheff and Mantelle cannot, without more, provide a basis for an obviousness rejection despite any recent revisions to the Manual of Patent Examining Procedure. As stated above, some articulated reason for combining those teachings with a reasonable expectation of success of arriving at the presently claimed subject matter is needed, independent of the mere recitation of ingredients in the prior art and/or the blueprint provided by the present Applicant's specification. The trade names Noveon® and Eudragit® are applied to a range of different polymers having a range of properties. As an example, the scope of the Eudragit® product line was brought to the Examiner's attention in the Appellant's response filed on February 8, 2010 (see *Exhibit 1* appended to that earlier response). Likewise, Mantelle acknowledges various polyacrylic acid polymers having different properties, and yet sold under the same mark (*Col. 6, ll 15-23*: "Particularly preferred are Carbopol® 934 NF, 934P NF, 940 NF and 971P NF.").

Indeed, as noted above, in the Action mailed on August 16, 2010 (*pg 3*) the Examiner himself took a similar position in rejecting certain claims of the application as uncertain in scope for including trade names/trademarks, arguing that "... the trademark or trade name cannot be used properly to identify any particular material or product." In view of the wide range of compositions marketed under the names Noveon® and Eudragit® (and the wide range of properties thereof), surely the same logic must apply to a Section 103 rejection, in that at least the requisite articulated reason for selecting and combining particular compositions cannot be derived from a mere recitation of trademarks. If inclusion of a trademark or trade name renders the scope of a claim so uncertain as to justify a rejection as indefinite, then in turn surely mere mention of the mark or trade name as one of a large number of recited compositions cannot of itself motivate the skilled artisan to combine selected compositions sold under that mark or trade name to arrive at a specific chemical composition having specific chemical properties.

Thus, Mantelle's (and the Examiner's) mere recitation of the trade names does not and cannot rise to the level of a teaching or articulated reason sufficient to provide the skilled artisan a reason to consider combining the teachings of Slavtcheff, Suzuki, and Mantelle to arrive at a pH-sensitive mucoadhesive layer bonded to a pharmaceutical wax layer as precisely set forth in the Appellant's independent claims. At most, what is provided is an invitation to experiment. Thus, even though Mantelle and Slavtcheff do list many compositions related to those of the Appellant's disclosure, no guidance is provided to lead the skilled artisan towards combining those compositions in the manner claimed by the Appellants, for the properties disclosed and claimed. For at least that reason, the rejection should be reversed.

2. Mantelle leads the skilled artisan away from use of anionic bioadhesive polymers as recited and claimed by the Appellant.

Moreover, rather than motivating the skilled artisan to select and combine compositions resulting in the subject matter of the Appellant's claims, Mantelle expressly leads the skilled artisan towards a combination of a significant excess of a neutral bioadhesive polymer (PVP and others) and "another" bioadhesive rather than the presently claimed combination of anionic polymers (Mantelle *Abstract*: "Bioadhesive compositions ... comprising a composition which results from an admixture of at least one PVP polymer, at least one bioadhesive, ...;" *Col. 4, ll 65 et seq.*: "... the inventors believe that the combination of PVP and another bioadhesive provides for a superior adhesion not attainable by either the PVP or another bioadhesive alone."). As stated in a previous response (Appellant's response filed on August 3, 2009, *pg 12*), PVP is a neutral polymer, and Mantelle also cites to compositions comprising ethyl cellulose, another neutral polymer. Mantelle further cites inclusion of PVP and other neutral polymers as specifically contributing to surprising results of its invention, stating that the combination of PVP and a polysaccharide bioadhesive, along with a solvent plasticizing the total composition, surprisingly resulted in a pressure-sensitive adhesive when neither

composition alone provided a pressure-sensitive adhesive (*Col. 36, ll 21-32*). Mantelle's inclusion of PVP is therefore neither optional nor incidental.

As set forth in the Appellant's specification and claims (see at least claims 34 and 44), a water-insoluble pharmaceutical wax layer is claimed at a concentration of 10% to 80% by weight of the total bioadhesive wax-film composite. Of that 10% to 80% by weight, 0.05% to 10% by weight may be a water soluble or swellable polymer (see claim 44), which polymer admittedly may be PVP (see claim 45). In contrast, however, Mantelle expressly teaches use of 5% to 50% by weight PVP, with those percentages reflecting percent by weight of the total Mantelle composition (see at least Mantelle *Col. 36, ll 36-44*). Accordingly, Mantelle requires significantly more of the neutral polymer to provide the advantageous properties of its two-bioadhesive composition, as compared to the Appellant's disclosure and claims requiring a significant excess of anionic polymers. Again, as discussed above, the skilled artisan in the chemical arts is well aware that even combining the same chemicals, in different proportions or under different conditions, results in compositions providing a wide variety of properties.

Thus, Mantelle does not motivate the skilled artisan to consider selecting bioadhesive anionic polymers as claimed by the Appellants, but rather guides the skilled artisan to inclusion of the neutral polymer in significant excess as compared to the Appellant's disclosure. In contrast, the Appellant has expressly claimed a pH-sensitive mucoadhesive polymer comprising at least one water soluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film-forming polymer, with significantly less weight-percent of any neutral polymer.

Moreover, in rebutting the Appellant's prior argument, the Examiner (Office Action mailed on August 16, 2010, *pg 8*) stated that "... Mantelle teaches an adhesive containing PVP, clearly PVP would not materially affect the basic and novel characteristic(s) of the claimed invention drawn to an adhesive since Mantelle uses this ingredient and the composition functions as an adhesive." Respectfully, this is a red

herring, and the Examiner apparently misapprehended the Appellant's argument. No suggestion was made that PVP is not an adhesive. The issue is that the Appellant's claims call for anionic polymers, and Mantelle expressly requires inclusion of a neutral polymer, preferably PVP, in significant excess compared to the Appellant's disclosure and claims. In making this rebuttal the Examiner merely puts forth an unsupported statement without supplying any evidence that inclusion of the neutral polymer would not "materially affect the basic and novel characteristics" of the presently claimed subject matter, that is, the claimed combination of anionic polymers for the properties described. This cannot rise to the level of the substantial evidence required to uphold an Office decision.

Even more, as discussed above the present claims call for a combination of a pH-sensitive mucoadhesive layer as claimed, bonded to a pharmaceutical wax layer. As is clear from the specification, the claimed molecule of interest can be delivered from either or both of the mucoadhesive layer and the wax layer. Nowhere in Mantelle is there any contemplation of delivery of a molecule from other than the mucoadhesive PVP/other bioadhesive composition, and Suzuki expressly teaches away from delivery of a molecule from its wax layer.

3. Summary.

No combination of Slavtcheff, Suzuki, or Mantelle teaches each and every limitation of the present independent claims. Likewise, no teaching of the references, express or inherent, articulates a reason leading the skilled artisan to combine the references to achieve the presently claimed combination. Still further, because of the wide range of compositions branded under the names Noveon® and Eudragit® as set forth in Mantelle and the wide range of properties thereof, the requisite reasonable expectation of success is lacking. The independent claims are believed to be in condition for allowance over the cited art under the propositions of *In re Ochiaie* and *KSR Int'l*, and the rejections should be reversed.

4. The dependent claims

The dependent claims are likewise believed to be allowable without consideration of obviousness under *In re Fritch* and *In re Fine*. Further, as set forth above in the discussion of the rejection of dependent claims over Slavtcheff and Suzuki (incorporated herein by reference as if fully restated), nowhere in the final Office Action mailed on January 14, 2011 or in any previous Office Action does the Examiner address many of the dependent claims with particularity and point to any teaching or suggestion of the references specifically believed to render the limitations of those dependent claims unpatentable. Therefore, *prima facie* obviousness of the dependent claims is not established, and the dependent claims are independently patentable.

The rejection of claims 33-34, 42-46, 51, 56, 57, and 63-68 over Slavtcheff, Suzuki, and Mantelle should be reversed.

D. THE REJECTION OF CLAIMS 33-34, 42-46, 56-57, AND 63-67 UNDER 35 U.S.C. §103(A) OVER MANTELLE IN VIEW OF SUZUKI.

1. Independent claims 33, 66, 67.

The discussion above of applicable law and the teachings of Mantelle and Suzuki is incorporated herein by reference as if fully restated. Again, for the reasons set forth above in section C rebutting the rejection over Slavtcheff/Suzuki/Mantelle, it is believed that no combination of the teachings of Mantelle and Suzuki provides any reason for the skilled artisan to contemplate the presently claimed combinations of a pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming copolymer, further wherein the pH-sensitive mucoadhesive layer is bonded to a pharmaceutical wax.

The lengthy teaching of ingredients set forth in Mantelle combined with the nonadhesive layer taught by Suzuki does not, without more, provide a basis for an obviousness rejection of the present claims despite the recent revisions to the Manual of

Patent Examining Procedure. Rather, some articulated reason for combining those teachings with a reasonable expectation of success of arriving at the presently claimed subject matter is needed, independent of the mere recitation of ingredients in the prior art and the blueprint provided by the present Applicant's specification.

As examples, the trade names Noveon® and Eudragit® are applied to a wide range of different polymers having an equally wide range of properties, and thus Mantelle's (and the Examiner's) mere recitation of the trade names does not and cannot rise to the level of a teaching or articulated reason sufficient to provide the skilled artisan motivation to consider combining the teachings of Mantelle and Suzuki to arrive at a pH-sensitive mucoadhesive layer as recited in the present amended independent claims. As stated by the Examiner himself, trade names/trademarks "cannot be used properly to identify any particular material or product," given the wide range of compositions branded under the names Noveon® and Eudragit® and the wide range of properties provided by those compositions. The required articulated reason for selecting particular combinations of compositions to arrive at the claimed pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming polymer as presently claimed is lacking, and it appears that the Examiner's position of obviousness constitutes the cautioned-against selective culling from the references in an attempt to fit the limitations of the claims, which is discouraged under the law.¹⁶

¹⁶ As is well established, virtually all inventions are combinations of old elements. *Ruiz v. A.B. Chance Co.*, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). It is improper to just find bits and pieces in the prior art and combine them whimsically to make rejections. Instead, it must be done "as a whole." *Id.* Otherwise, "an obviousness assessment might break an invention into its component parts (A+B+C), then find a prior art reference containing A, another containing B, and another containing C, and on that basis alone declare the invention obvious." *Id.* In turn, "this form of hindsight reasoning, using the invention as a roadmap to find its prior components, would discount the value of combining various existing features or principles in a new way to achieve a new result - often the very definition of invention." *Id.* The U.S. Supreme Court affirmed this rationale in *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007) when it said "[a]s is clear from cases such as *Adams*, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art."

In turn, Suzuki provides no inkling of any element of bonding a wax (or any other recited nonadherent layer) to its bioadhesive layer whereby a molecule of interest may be delivered to a mucosal surface from either of the bioadhesive layer or the wax layer. Rather, Suzuki expressly avoids inclusion of a medicament or other molecule of interest in its nonadherent layer. In contrast, the present disclosure and claims set forth that exact subject matter.

Further, as set forth in detail above, Mantelle requires an excess of a neutral bioadhesive polymer (PVP) as compared to the Appellant's disclosure and claims. Inclusion of PVP is advocated as providing superior bioadhesive properties to Mantelle's composition comprising at least two bioadhesive materials (*Col. 2, ll 30-36*), and consistently Mantelle requires inclusion of a soluble PVP polymer (see the various bioadhesive embodiments of Mantelle set forth at *Col. 2-4*) at a weight % of 5% to 50% of the total bioadhesive composition (*Col. 36, ll 36-44*), compared to the present disclosure. The Examiner provides no evidence that inclusion of the excess of neutral polymer advocated by Mantelle would not materially alter the properties of the Appellant's claimed bi-layer wax-film composite comprising primarily anionic polymers.

For at least those reasons, set forth in greater detail above, the combination of Mantelle and Suzuki fails to teach or provide an objective reason for the skilled artisan to consider implementing each and every limitation of the present claims. Further, no combination of the references provides the required reasonable expectation of success. The rejection should be reversed.

2. The dependent claims

The dependent claims are likewise believed to be allowable without consideration of obviousness over Mantelle and Suzuki under the proposition set forth in *In re Fritch* and *In re Fine*. Further, as set forth above in the discussion of the rejection of dependent claims over Slavtcheff and Suzuki (incorporated herein by reference as if fully restated), the Examiner fails to address many of the dependent claims with particularity and point

to any teaching or suggestion of the references believed to render the dependent claims unpatentable. Therefore, *prima facie* obviousness of the dependent claims is not established, and the dependent claims are independently patentable.

The rejection of claims 33-34, 42-46, 56-57, and 63-67 over Mantelle in view of Suzuki should be reversed.

E. CONCLUSION

The Appellant submits, for the reasons set forth above: (1) that no reasonable interpretation of the cited references, alone or in combination, teaches or suggests each and every limitation of the claims under consideration, and therefore the asserted combination of references does not support *prima facie* obviousness of the claims; (2) that no reason is articulated for the skilled artisan to consider combining the references to arrive at the claimed subject matter, and therefore *prima facie* obviousness of the claims is unsupported; (3) that no reasonable expectation of success of the combination of reference features asserted by the Examiner is provided to the skilled artisan, and therefore *prima facie* obviousness of the claims is unsupported; and (4) that for the flaws in the rejections as set forth above, all the pending claims are in condition for allowance. It is respectfully requested that the rejections of the pending claims be reversed and that the application be remanded to the Examiner for issuance of a prompt Notice of Allowance.

Also, in the Office Action mailed on February 2, 2004, the Examiner required restriction to a number of species relating to the claim limitation of “at least one molecule of interest.” In that Action (*pg* 3, at top), the Examiner acknowledged that “a claim for ‘a wax-film composite’ is generic” to those species. It is believed that the generic claim (claim 33) to the wax film composite is in condition for allowance. Therefore, it is respectfully requested that the Examiner also be directed to rejoin and allow claims 47-50

and 52-55 directed to other identified species of molecule of interest, each of which depends from claim 33 and incorporates its limitations by reference.

Finally, to the extent any fees are due beyond those authorized in the fee transmittals for filing a brief in support of a Notice of Appeal, the undersigned authorizes the Commissioner to charge fees and credit overpayments to **Deposit Account No. 11-0978**.

Respectfully submitted,

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VIII. CLAIMS APPENDIX

The claims on Appeal are 33-34, 42-46, 51, 56-57, and 63-68. Of those, claims 1 and 19 appear as previously presented while claims 2-4 and 20-25 remain as originally presented. Claims 47-50 and 52-55 have been withdrawn from consideration, but are set forth below for the Board's convenience. Claims 1-32, 35-41, and 58-62 were canceled without prejudice during prosecution before the Examiner.

Listing of Claims:

1-32 (Canceled).

33. (Previously presented) A bi-layer wax-film composite having a total thickness of less than 5 mm, comprising:

(a) a pH-sensitive mucoadhesive layer, comprising:

(1) at least one water-insoluble swellable anionic mucoadhesive polymer;

and

(2) at least one anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester;

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer; and

(c) at least one molecule of interest;

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto.

34. (Original) The wax-film composite of claim 33, wherein the pH-sensitive mucoadhesive layer is present at a concentration of 20% to 90% by weight, and the water-insoluble wax layer is present at a concentration of 10% to 80% by weight.

35-41. (Canceled).

42. (Original) The wax-film composite of claim 33, wherein the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax having a melting point between 40° C and 100° C and at least one water-soluble or water-swellaable polymer.

43. (Previously presented) The water-insoluble pharmaceutical wax of claim 42, wherein said wax is beeswax, emulsifying wax, microcrystalline wax, carnauba wax, paraffin wax, white wax, yellow wax, or other suitable pharmaceutical wax.

44. (Previously Presented) The water-soluble or swellable polymer of claim 42, wherein said polymer is present in the insoluble wax layer at a concentration from 0.05% to 10% by weight.

45. (Original) The water-soluble or swellable polymer of claim 42, wherein said water-soluble or water-swellaable polymer is tragacanth, polyvinyl pyrrolidone, polyvinyl

alcohol, cross-linked polyacrylic acid, polyethylene glycol, a cellulose polymer derivative, or other suitable pharmaceutical polymer that is water-soluble or water-swellaable.

46. (Previously presented) The wax-film composite of claim 33, wherein the molecule of interest is contained in and released from either the pH-sensitive mucoadhesive layer or the water-insoluble wax layer.

47. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest comprises an active pharmaceutical compound, a sweetener, a flavoring agent, a diagnostic agent, or a combination thereof.

48. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is amlexanox.

49. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is triclosan.

50. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is lidocaine, benzocaine, or dyclonine.

51. (Previously presented) The wax-film composite of claim 33, wherein the molecule of interest is a peptide or protein.

52. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is at least one benzodiazepine drug or derivative thereof.

53. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is hirudin or hirudin complexed with a substance of opposite charge.

54. (Withdrawn) The wax-film composite of claim 53, wherein said substance of opposite charge is chitosan or protamine.

55. (Withdrawn) The wax-film composite of claim 33, wherein the molecule of interest is plasmid DNA or plasmid DNA complexed with a substance of opposite charge such as chitosan, protamine, or a cationic lipid.

56. (Previously Presented) The wax-film composite of claim 33, wherein the wax-film composite is applied to an application site comprising: the skin, mouth, vagina, nasal cavity, or other accessible mucosal site.

57. (Previously Presented) The wax-film composite of claim 56, wherein the wax-film composite adheres to the application site for at least one hour.

58-62. (Canceled)

63. (Previously presented) The wax-film composite of claim 33, wherein the weight ratio of water-insoluble swellable anionic mucoadhesive polymer to anionic pH-sensitive film-forming copolymer is from 2:1 to 4:1.

64. (Previously presented) The wax-film composite of claim 47, wherein the active pharmaceutical compound is an antimicrobial, an antiviral, an antiinflammatory, an antiseptic, an antihistamine, a local anesthetic, a disinfectant, a keratolytic, an analgesic, an anti-migraine or an antifungal.

65. (Previously presented) The wax-film composite of claim 33, wherein the water-insoluble wax layer comprises at least one water-insoluble pharmaceutical wax having a melting point between 40° C and 100° C.

66. (Previously presented) A bi-layer wax-film composite having a total thickness of less than 5 mm, comprising:

(a) a pH-sensitive mucoadhesive layer, comprising:

- (1) at least one water-insoluble swellable anionic mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol; and
- (2) at least one anionic pH-sensitive film-forming polymer copolymer of methacrylic acid and acrylic or methacrylic ester;

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer; and

(c) at least one molecule of interest;

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto.

67. (Previously presented) A bi-layer wax-film composite having a total thickness of less than 5 mm, comprising:

(a) a pH-sensitive mucoadhesive layer, consisting essentially of:

- (1) at least one water-insoluble swellable anionic mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol; and
- (2) at least one anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester;

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer; and

(c) at least one molecule of interest;

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto.

68. (Previously presented) A bi-layer wax-film composite having a total thickness of less than 5 mm, comprising:

(a) a pH-sensitive mucoadhesive layer, consisting of:

(1) at least one water-insoluble swellable anionic mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol; and

(2) at least one anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester;

(b) a water-insoluble pharmaceutical wax layer bonded to the pH-sensitive mucoadhesive layer; and

(c) at least one molecule of interest;

wherein the pH-sensitive mucoadhesive layer adheres to a wet mucosal surface for delivery of the molecule of interest thereto.

IX. EVIDENCE APPENDIX

None

X. RELATED PROCEEDINGS APPENDIX

None